

Claim 4 (amended) Compounds of formula II_A according to claim 2 and corresponding to the following formulae:

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(5R)-5-ethyl-8-fluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino[1,2-b]quinoleine-3,15-dione ;

(5R)-5-ethyl-9,10-difluoro-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7]indolizino[1,2-b]quinoleine-3,15-dione ;

(5R)-5-ethyl-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino[1,2-b]quinoleine-3,15-dione ;

(5R)-12-decyl-5-ethyl-9-fluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7]indolizino [1,2-b]quinoleine-3,15-dione ;

(5R)-12-decyl-5-ethyl-9,10-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7]indolizino [1,2-b]quinoleine-3,15-dione ;

(5R)-12-decyl-5-ethyl-9,11-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7]indolizino [1,2-b]quinoleine-3,15-dione ;

(5R)-5-ethyl-9-fluoro-5-hydroxy-12-(4-trifluoromethoxyphenyl)-4,5,13,15-tetrahydro-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinoleine-3,15-dione ;

(5R)-12-(4-dimethylaminophenyl)-5-ethyl-9-fluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinoleine-3,15-dione ;

(5R)-5-ethyl-9-fluoro-5-hydroxy-3,15-dioxo-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7]indolizino[1,2-b]quinolein-10-yl trifluorometanesulfonate.

Claim 10 (amended) As medicament, a compound of formula (I) or (II_A) according to claim 1 or a therapeutical salt thereof.

Claim 12 (amended) Pharmaceutical compositions containing at least one of the compounds as defined in claim 1 as an active ingredient.

Cancel claims 13 to 16 and add the following claims.

--19. A method of inhibiting topoisomerases in warm-blooded animals comprising administering to warm-blooded animals in need thereof an amount of a compound of ^{claim 23}~~claim 1~~ sufficient to inhibit topoisomerases.

20. A method of treating tumors in warm-blooded animals comprising administering to warm-blooded animals in need thereof an antitumor effective amount of a compound of ^{claim 23}~~claim 1~~.

21. A method of treating viral infections in warm-blooded animals comprising administering to warm-blooded animals in need thereof an antivirally effective amount of a compound of ^{claim 23}~~claim 1~~.

22. A method of treating parasitic infections in warm-blooded animals comprising administering to warm-blooded animals in need thereof an antiparasitically effective amount of a compound of ^{claim 23}~~claim 1~~--

AB
Claim 10 (amended) As medicament, a compound of formula (I) or (II_A) according to claim 1 or a therapeutical salt thereof.

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Claim 12 (amended) Pharmaceutical compositions containing at least one of the compounds as defined in claim 1 as an active ingredient.

Cancel claims 13 to 16 and add the following claims.

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--19. A method of inhibiting topoisomerases in warm-blooded animals comprising administering to warm-blooded animals in need thereof an amount of a compound of claim 1 sufficient to inhibit topoisomerases.

20. A method of treating tumors in warm-blooded animals comprising administering to warm-blooded animals in need thereof an antitumor effective amount of a compound of claim 1.

21. A method of treating viral infections in warm-blooded animals comprising administering to warm-blooded animals in need thereof an antivirally effective amount of a compound of claim 1.

22. A method of treating parasitic infections in warm-blooded animals comprising administering to warm-blooded animals in need thereof an antiparasitically effective amount of a compound of claim 1.--

3. Compounds according to claim 1 ~~or 2~~ in which R₁ represents an ethyl radical.

4. Compounds of formula II_A according to claim 2 ~~or 3~~ and corresponding to the following formulae :

- 5 (5R)-5-ethyl-8-fluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino[1,2-b]quinoleine-3,15-dione ;
- (5R)-5-ethyl-9,10-difluoro-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7]indolizino[1,2-b]quinoleine-3,15-dione ;
- (5R)-5-ethyl-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino[1,2-b]quinoleine-3,15-dione ;
- 10 (5R)-12-decyl-5-ethyl-9-fluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7]indolizino [1,2-b]quinoleine-3,15-dione ;
- (5R)-12-decyl-5-ethyl-9,10-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7]indolizino [1,2-b]quinoleine-3,15-dione ;
- (5R)-12-decyl-5-ethyl-9,11-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7]indolizino [1,2-b]quinoleine-3,15-dione ;
- 15 (5R)-5-ethyl-9-fluoro-5-hydroxy-12-(4-trifluoromethoxyphenyl)-4,5,13,15-tetrahydro-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinoleine-3,15-dione ;
- (5R)-12-(4-dimethylaminophenyl)-5-ethyl-9-fluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinoleine-3,15-dione ;
- 20 (5R)-5-ethyl-9-fluoro-5-hydroxy-3,15-dioxo-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7]indolizino[1,2-b]quinolein-10-yl trifluorometanesulfonate.

5. Compounds of formula II_A according to claim 4 and corresponding to the following formulae :

- 25 (5R)-5-ethyl-9,10-difluoro-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7]indolizino[1,2-b]quinoleine-3,15-dione ;
- (5R)-5-ethyl-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino[1,2-b]quinoleine-3,15-dione.

6. Compounds of formula I according to claim 1 and corresponding to the following formulae :

5

R₇, R₈ and R₉

R₁₀

10

m

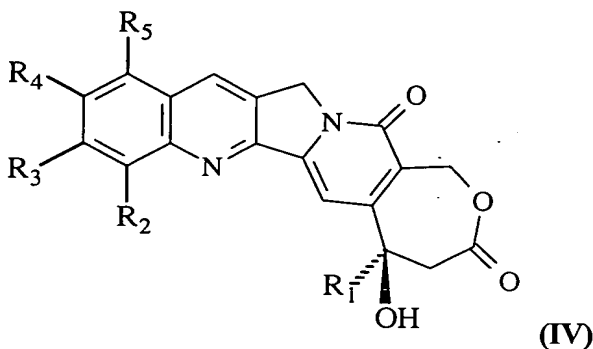
radicals identical or different, lower hydroxy alkyl, lower alkoxy lower alkyl, lower cycloalkyl alkyl, $-(CH_2)_mSiR_7R_8R_9$ radical, or lower aryl alkyl radical substituted or non substituted on the aryl group, the substituents being identical or different and selected from : a lower alkyl, a hydroxy group, halo, amino, lower alkyl amino, di(lower alkyl)amino, CF₃ or OCF₃ ;

represent, independently, a lower alkyl radical ;

represents a lower alkyl radical optionnally substituted by one or more halo radicals identical or different, or an aryl optionnally substituted by one or more lower alkyl radicals identical or different ;

is an integer comprised between 0 and 6 ;

said process characterized in that a compound of formula



15 in which R₁, R₂, R₃, R₄ and R₅ have the meaning indicated above, is treated in a strongly acid medium in the presence of an iron (III) salt and a precursor of the free radical R₆[•], by a solution containing hydroxide or alkoxide radicals.

10. As medicament, a compound of formula (I) or (II_A) according to claims 1 to 8 or a therapeutical salt thereof.

11. As medicament, a compound of formula (III) according to claim 9, or a therapeutical salt thereof.

12. Pharmaceutical compositions containing at least one of the compounds as defined in claims 1 to 8 as an active ingredient.

13. Use of the compounds according to claims 1 to 8 for the preparation of medicaments intended to inhibit topoisomerases, and more particularly the topoisomerases of type I or of type II.

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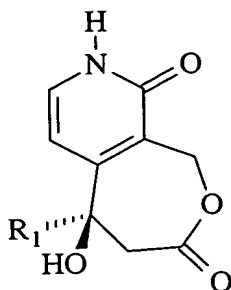
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14. Use of the compounds according to claims 1 to 8 for the preparation of medicaments to treat tumors.

15. Use of the compounds according to claims 1 to 8 for the preparation of medicaments intended to treat viral infections or diseases.

5 16. Use of the compounds according to claims 1 to 8 for the preparation of medicaments intended to treat parasitic infections.

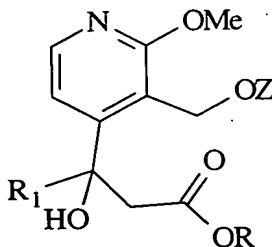
17. As a new industrial product, a compound of general formula M



wherein R₁ represents a lower alkyl radical.

10 18. Process for the preparation of a compound of formula M according to claim 17, said process including the following successive stages :

- a racemic ester represented below



15 in which R₁ has the meaning indicated in claim 17, R is a lower alkyl and Z a protective group of the alcohol function is converted to the corresponding carboxylic acid ;

- this compound is then subjected to an operation which separates the enantiomers, known to the person skilled in the art under the name of resolution and which allows an enantiomerically enriched compound of general formula

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